Please replace the paragraph starting at page 3, line 14 with the following:

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1- C_3)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, Ar_1 ~~(~~wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6- membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine, ~~(~~wherein the ring fusion is at a carbon-carbon double bond of Ar~~)~~~~)~~, Ar-alkyl, Ar-O, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy; or

Please replace the paragraph starting at page 6, line 30 with the following:

[c] R^9 is hydrogen or lower alkyl, and R^{10} is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur~~, said heterocycle~~; or

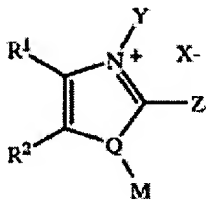
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended A method of treating, ~~or~~ ameliorating or preventing ~~an indication of the invention~~ hypertension or systolic hypertension in an animal, including a human, comprising administering

(A) an effective amount of an antioxidant, angiotensin converting enzyme (ACE) inhibitor, angiotensin II receptor antagonist, calcium channel blocker, diuretic, digitalis, beta blocker, statin or cholestyramine; and

(B) an effective amount of ~~(A)~~ a compound of the formula I:



(I)

wherein

a. R^1 and R^2 are

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1- C_3)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, Ar, ~~wherein~~, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one

to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine, ~~(~~wherein the ring fusion is at a carbon-carbon double bond of Ar~~)~~, Ar-alkyl, Ar-O, $ArSO_2$-, ArSO-, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy; or

2. together with their ring carbons form a C_6- or C_{10}-aromatic fused ring system; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the -olium or -onium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or

4. together with their ring carbons form a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-pyrrolidinyl-, 4-[C_6 or C_{10}] arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3)alkylenedioxy groups; or

5. together with their ring carbons form a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and $S(O)_n$, where n=0, 1, or 2;

b. Z is

1. hydrogen, alkyl, or Ar-CH_2;

~~2. a group of the formula $-NR^3R^4$, wherein R^3 and R^4 may be independently hydrogen, alkyl, Ar, or Ar-alkyl;~~

~~3. a group of the formula $-CH(OR^{11})R^{12}$, wherein R^{11} is hydrogen, methyl, ethyl or $CH_3C(O)$; and R^{12} is [C_1 to C_6]alkyl, Ar, or CO_2R^{13} wherein R^{13} is hydrogen methyl or ethyl;~~

~~4. a group of the formula $-C(CO_2R^{13})(OR^{11})R^{12}$~~

~~5. a group of the formula $-CH_2WAr$, wherein W is $-(C=O)-$ or $-S(O)_n-$ where n=1 or 2; or~~

~~6. a group of the formula $-CH_2C\equiv C-R^{14}$, wherein R^{14} is (C_1-C_6)alkyl;~~

c. Y is

~~1. amino, or~~

2. a group of the formula $-CH(R^5)-R^6$, wherein

(a) R^5 is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, dialkylaminoalkyl-, (N-[C_6 or C_{10}]aryl)(N-alkyl) aminoalkyl-, piperidin-1-ylalkyl-, 1-pyrrolidinylalkyl, azetidinylalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4-[C_6 or C_{10}]arylpiperazin-1-ylalkyl, 4-[C_6 or C_{10}]arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl, [C_6 or C_{10}]aryl, or independently the same as R^6;

(b) R^6 is

(1) hydrogen, alkyl (which can be substituted by alkoxycarbonyl), alkenyl, alkynyl, cyano- or Rs, wherein Rs is a C_6 or C_{10} aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

(2) a group of the formula $-W-R^7$, wherein R^7 is alkyl, alkoxy, hydroxy or Rs, wherein W is $-C(=O)-$ or $-S(O)_n-$ where n=1 or 2;

(3) a group of the formula -W-OR^8 wherein R^8 is hydrogen or alkyl,

(4) a group of the formula -CH(OH)Rs; or

(5) a group of the formula -W-$N(R^9)R^{10}$, wherein [a] R^9 is hydrogen and R^{10} is an alkyl or cycloalkyl, optionally substituted by (i) [C_6 or C_{10}]aryl, or (ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3) alkylenedioxy groups, or fused to a substituted phenyl or pyridine ring, wherein the ring fusion is at a carbon-carbon double bond of the heteroaryl ring, or (iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or [b] R^9 is hydrogen or lower alkyl and R^{10} is Ar; or [c] R^9 is hydrogen or lower alkyl, and R^{10} is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur, said heterocycle; or [d] R^9 and R^{10} are both alkyl groups; or [e] R^9 and R^{10} together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C_6- or C_{10})aryl, (C_6- or C_{10})arylalkyl, or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and

zero to two atoms of N, each such heteroaryl can be optionally substituted with one or more

1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}] arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3)alkylenedioxy; or [f] R^9 and R^{10} are both hydrogen; or

d. Q is ~~N, O or~~ S;

e. M is absent ~~when Q is O or S~~; and

~~f. M is alkyl, vinyl or allyl, or independently the same as Y; and~~

g. X is a pharmaceutically acceptable anion, or

(~~B~~ C) a pharmaceutically acceptable salt of the compound,
wherein aryl or Ar can be substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, ArO-, Ar-, Ar-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin- 4-yl, piperidin-1-yl; and
wherein heterocycles, except those of Ar, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

2. (Original) The method of claim 1, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula - $CH(R^5)R^6$.

3. (Original) The method of claim 2, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula - $CH(R^5)$-W-R^7.

4. (Original) The method of claim 2, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula - $CH(R^5)$-W-Rs.

5. (Cancelled) ~~The method of claim 1, comprising administering an effective amount of a compound of formula I, wherein R^1 and R^2 together with their ring carbons form a C_6- or C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfonic acid, alkylsulfonyl or ω-alkylenesulfonic acid groups, or a C_1-C_3 alkylenedioxy group with the proviso that when Q is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring.~~

6. (Cancelled) ~~The method of claim 1, comprising administering an effective amount of a compound of the compound of formula I, wherein Q is S, and Y and Z are both NH_2.~~

7. (Currently Amended) The method of claim 1, comprising administering an effective amount of a compound of formula I, wherein

a. R^1 and R^2 are

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C_1-C_3)alkylenedioxy, allyl, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, Ar, ~~(~~wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6- membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a benzene, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine, ~~(~~wherein the ring fusion is at a carbon- carbon double bond of Ar~~)~~, Ar-alkyl, Ar-O, $ArSO_2$-, ArSO-,

ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O) NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-; or

2. together with their ring carbons form a C_6- or C_{10}-aromatic fused ring system; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the -olium or -onium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, aminocarbonyl, carboxy, fluoro, or oxo substituents; or

4. together with their ring carbons form a 5- or 6- membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more halo or (C_1-C_3)alkylenedioxy groups; or

5. together with their ring carbons form a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and $S(O)_n$, where n=0, 1, or 2;

b. Z is

1. hydrogen, alkyl, or Ar-CH_2;

~~2. a group of the formula $-NR^3R^4$, wherein R^3 and R^4 may be independently hydrogen, alkyl, Ar, or Ar-alkyl ;~~

~~3. a group of the formula $-CH(OR^{11})R^{12}$, wherein R^{11} is hydrogen, methyl, ethyl or $CH_3C(O)$; and R^{12} is [C_1 to C_6]alkyl, Ar, or CO_2R^{13} wherein R^{13} is hydrogen methyl or ethyl;~~

~~4. a group of the formula $-C(CO_2R^{13})(OR^{11})R^{12}$~~

~~5. a group of the formula $-CH_2WAr$, wherein W is $-(C=O)-$ or $-S(O)_n-$ where n=1 or 2; or~~

~~6. a group of the formula $-CH_2C\equiv C-R^{14}$, wherein R^{14} is (C_1-C_6)alkyl;~~

c. Y is

~~1. amino, or~~

2. a group of the formula $-CH(R^5)-R^6$ wherein

(a) R^5 is hydrogen or alkyl;

(b) R^6 is

(1) hydrogen, alkyl (which can be substituted by alkoxycarbonyl), alkenyl, alkynyl, cyano- or Rs, wherein Rs is a C_6 or C_{10} aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

(2) a group of the formula $-W-R^7$, wherein R^7 is alkyl, alkoxy, hydroxy or Rs, wherein W is –C=O- or $-S(O)_n-$ where n=1 or 2;

(3) a group of the formula $-W-OR^8$ wherein R^8 is hydrogen or alkyl,

(4) a group of the formula -CH(OH)Rs; or

(5) a group of the formula $-W-N(R^9)R^{10}$, wherein [a] R^9 is hydrogen and R^{10} is an alkyl or cycloalkyl, optionally substituted by (i) [C_6 or C_{10}]aryl, or (ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more halo or

(C_1-C_3) alkylenedioxy groups, or fused to a substituted phenyl, or (iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or [b] R^9 is hydrogen or lower alkyl and R^{10} is Ar; or [c] R^9 is hydrogen or lower alkyl, and R^{10} is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur, said heterocycle; or [d] R^9 and R^{10} are both alkyl groups; or [e] R^9 and R^{10} together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C_6- or C_{10})aryl, (C_6- or C_{10})arylalkyl, or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each such heteroaryl can be optionally substituted with one or more halo or (C_1-C_3)alkylenedioxy; or [f] R^9 and R^{10} are both hydrogen; or

d. Q is ~~N, O or~~ S;

e. M is absent ~~when Q is O or S~~; and

~~f. M is alkyl, vinyl or allyl, or independently the same as Y; and~~

g. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,

wherein aryl or Ar can be substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C_1-C_3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, ArC(O)-, ArC(O)NH-, ArO-, Ar- , Ar-alkyl-,

carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid; and

wherein heterocycles, except those of Ar, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, ArC(O)-, ArO-, Ar-, carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

8. (Original) The method of claim 7, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula - $CH(R^5)R^6$.

9. (Original) The method of claim 8, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula - $CH(R^5)$-W-R^7.

10. (Original) The method of claim 8, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -$CH(R^5)$-W-Rs.

11. (Cancelled) ~~The method of claim 7, comprising administering an effective amount of a compound of the compound of formula I, wherein Q is S, Y and Z are both NH_2.~~

12. (New) The method of claim 1, wherein the compound is 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt.

13. (New) The method of claim 12, wherein the compound is 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium chloride.

14. (New) The method of claim 12, wherein the compound is 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium bromide.